

Turning to the Office action, the Examiner maintains the rejection of Claim 22 under 35 U.S.C. § 112, first paragraph, for reasons given on page 2 of the Office action. Without further comment on the merits of the rejection but to expedite prosecution towards an allowance, Applicants are complying with the Examiner's kind suggestion to incorporate the specific diseases of Claim 23 into Claim 22. Claim 23 is canceled. As a result of the amendment, it is respectfully asked that the Examiner withdraw the rejection and allow Claim 22.

Although the Office action is silent as to the disposition of Claims 24-31, the working examples in the specification support the patentability of these claims. The examples sufficiently demonstrate that the compounds of the invention inhibit numerous kinase pathways such as EGFR or erbB2 (Her2) on pages 124-126 (Claim 24); MAPK on pages 127-128 (Claim 25); RAF kinase on pages 136-140 (Claim 26); SRC kinase on pages 128-129 (Claim 27); Mek-Erk on pages 127-130 (Claim 28); and VEGF/KDR on pages 126-130 (Claim 29). Insofar as Claim 30 (polycystic kidney disease) is concerned, there is an established correlation that deregulation of the EGF receptors is a factor in the growth of epithelial cysts in polycystic kidney disease (see discussion in the specification on page 2, lines 20-26). It is reasonable for one of ordinary skill in the art to predict that the compounds of the present invention, which are shown to inhibit the catalytic function of the EGF receptors, are useful for the treatment of polycystic kidney disease. Regarding Claim 31 (colonic polyps), the working examples illustrate biological activity against a wide range of carcinogenic cell lines affecting the colon such as HT-29 and Ca-CO2 (colorectal adenocarcinoma) on pages 132-134; and SW620 and LoVo (colon cancer) on pages 134-136 and 138-140, respectively. The evidence clearly permits one of ordinary skill in the art to conclude that the compounds are useful in the treatment of colonic polyps. Therefore, it is respectfully requested that Claims 24-31 be held allowable.

With respect to the objection to Claims 32 and 33, the Examiner believes that defining diseases by the underlying cause renders the scope of the intended uses indeterminate. While the Examiner's kind suggestion to cancel the two claims to place the case in condition for allowance is greatly appreciated, Applicants respectfully disagree with the necessity to omit these claims and ask the Examiner to please reconsider in view of the following remarks.

Claims 32 and 33 are not simply defining a disease by the underlying cause. Rather, the claims are drawn to a method of treatment on a molecular level that is known in the art and

well documented to be correlated to certain diseases. For instance, the biological effects of a deregulated protein kinase are shown by uncontrolled cell proliferation, which leads to tumor growth and cancer (see discussion in the specification on page 1, lines 22-27) and the growth of epithelial cysts in polycystic kidney disease (see page 2, lines 20-26). Furthermore, a defect in a signaling pathway upstream from a protein kinase is implicated in colon cancer; overexpression of a protein kinase is implicated in lung cancer and colonic polyps; and a dysregulated protein kinase is implicated in glioblastoma, among other neoplasms (see discussion on page 123, lines 1-24, explaining the utility based on the art-recognized correlation and the list of other protein kinase-associated disease states (in addition to neoplasms) on page 123, lines 16-24, in which treatment would benefit from the use of the compounds of this invention). As a result of the known etiology, these disease states that relate to protein kinase can be treated or inhibited by protein kinase inhibitors. Hence, one of ordinary skill in the art would conclude that the novel compounds of the present invention that demonstrate excellent broad-spectrum activity by inhibiting numerous kinase pathways in a variety of standard pharmacological test procedures can be used to treat or inhibit diseases caused by a deregulated protein kinase, defective pathway, *etc.*

There is also precedent in the claim language of issued patents to show that the scope of Claims 32 and 33 would be definite and understood by those of ordinary skill in the art. The parent U.S. Patent No. 6,638,929 (Claims 14 and 15) is a good example since the teachings in the prior case and the instant application are the same. Additionally, U.S. Patent Nos. 6,689,772 (Claims 22 and 23); 6,548,496 (Claim 4); 6,251,912 (Claim 13); 6,002,008 (Claim 21); and 5,760,041 (Claim 15) prove that the scope of the intended use of instant Claims 32 and 33 are instantly recognizable by those skilled in the art.

In view of the foregoing remarks and the proffered evidence, Applicants respectfully request that the Examiner allow Claims 32 and 33 in the present application.

Finally, clarification of the claims that were examined is respectfully requested to guarantee that the correct claims are allowed in this case. Specifically, the exact status of Claims 24-31, 34 and 36 is unclear. The Detailed Action indicates that Claims 1, 10, 19, 20, 22-34 and 36 are pending; and Claims 1, 10, 19 and 20 are allowed. On the other hand, the Office Action Summary confirms that Claims 1, 10, 19 and 20 are allowed but then specifies that Claims 23-34

are withdrawn from consideration. Since the Office Action does deal expressly with Claims 23, 32 and 33, it is certain that these three claims have been examined. The complete record, however, does not reflect an accurate representation of all of the examined and allowed subject matter.

Most importantly, it makes sense that the pharmaceutical composition of Claim 34 would be allowed in view of allowed Claim 1 but there is no confirmation that Claim 34 is allowed. Claim 36, which recites the process of making the allowed compounds, was presented to address the Examiner's concern that process Claim 35 incorporated flow sheets by reference to the specification. Since there is no apparent rejection of Claim 36, it seems likely that the claim would be allowed but Claim 36 was not included in any list of allowed claims. Lastly, the Office action is silent as to the status of pending Claims 24-31, that is, whether these claims are considered allowable but for their dependence on a rejected base claim. Thus, Applicants respectfully ask that the next Official action on the merits clarifies the record or, in the preferred alternative, that the Notice of Allowability properly identifies the allowance of Claims 1, 10, 19, 20, 22, 24-34 and 36.

The Examiner is again encouraged to contact the undersigned attorney to discuss any outstanding issues in this case.

Accordingly, favorable treatment is respectfully urged and appreciated.

Respectfully submitted,

WYETH

Date: September 15, 2005

By: Anne M. Rosenblum
Anne M. Rosenblum
Attorney for Applicants
Registration No. 30,419

FILING BY EXPRESS MAIL UNDER 37 C.F.R. § 1.10

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Anne M. Rosenblum
Anne M. Rosenblum